0			2002/12/0 4 07:20	USPAT; US-PGPUB; EPO; JPO; DERWENT	6 same (7 or 8 or 9)	0	L10	BRS	10
0			2002/12/0	USPAT; US-PGPUB; EPO; JPO; DERWENT	protease adj nexin\$1	342	L9	BRS	9
0			2002/12/0 4 07:20	USPAT; US-PGPUB; EPO; JPO; DERWENT	heparin adj binding adj domain	314	L8	BRS	8
0			2002/12/0 4 07:19	USPAT; US-PGPUB; EPO; JPO; DERWENT	glycosaminoglycan	4175	L7	BRS	7
0			2002/12/0 4 07:19	USPAT; US-PGPUB; EPO; JPO; DERWENT	5 same (chimeric or fusion)	4	L6 .	BRS	0
0			2002/12/0 4 07:01	USPAT; US-PGPUB; EPO; JPO; DERWENT	(1 or 2) same (3 or 4)	68	L5	BRS	Ŋ
0			2002/12/0 4 07:00	USPAT; US-PGPUB; EPO; JPO; DERWENT	kunitz same (domain adj 2)	20	L4	BRS	44
0			2002/12/0 4 07:00	USPAT; US-PGPUB; EPO; JPO; DERWENT	kunitz same (domain adj 1)	8 6	L3	BRS	ω
0			2002/12/0 4 06:59	USPAT; US-PGPUB; EPO; JPO; DERWENT	TFPI-2	50	L2	BRS	Ν
0			2002/12/0 4 06:59	USPAT; US-PGPUB; EPO; JPO; DERWENT	TFPI	403	L1	BRS	Ľ
R C F	Err or Def ini tio	Com men ts	Time Stamp	DBs	Search Text	Hits	# #	Туре	

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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT

07:23:45 ON 04 DEC 2002

- L1 3347 S TFPI
- L2 221 S TFPI-2
- L3 42 S KUNITZ (P) (DOMAIN 1)
- L4 32 S KUNITZ (P) (DOMAIN 2)
- L5 30 S (L1 OR L2) (P) (L3 OR L4)
- L6 2 S L5 (P) (CHIMERIC OR FUSION)
- L7 2 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
- L8 70335 S GLYCOSAMINOGLYCAN
- L9 2924 S HEPARIN BINDING DOMAIN
- L10 728 S PROTEASE NEXIN-1
- L11 3 S L9 (P) L10
- L12 1 S L7 (P) (L8 OR L11)

 $=> \log y$ 

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=> file medline caplus biosis embase scisearch agricola
                                                 SINCE FILE
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COST IN U.S. DOLLARS
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                                                      ENTRY
                                                       0.21
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=> s tfpi
          3347 TFPI
=> s tfpi-2
           221 TFPI-2
=> s kunitz (p) (domain 1)
            42 KUNITZ (P) (DOMAIN 1)
   s kunitz (p) (domain 2)
=>
            32 KUNITZ (P) (DOMAIN 2)
=> s (11 or 12) (p) (13 or 14)
            30 (L1 OR L2) (P) (L3 OR L4)
=> s 15 (p) (chimeric or fusion)
             2 L5 (P) (CHIMERIC OR FUSION)
=> duplicate remove 16
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L6
              2 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
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     ANSWER 1 OF 2 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
T.7
ACCESSION NUMBER:
                    2001:340475 BIOSIS
                    PREV200100340475
DOCUMENT NUMBER:
                    Chimeric proteins.
TITLE:
AUTHOR (S):
                    Innis, Michael A.; Creasey, Abla A.
                    ASSIGNEE: Chiron Corporation
PATENT INFORMATION: US 6174721 January 16, 2001
                    Official Gazette of the United States Patent and Trademark
SOURCE:
                    Office Patents, (Jan. 16, 2001) Vol. 1242, No. 3, pp. No
                    Pagination. e-file.
                    ISSN: 0098-1133.
DOCUMENT TYPE:
                    Patent
LANGUAGE:
                    English
                                             ***Kunitz*** -type
       ***Chimeric***
                        proteins possessing
                        ***1*** of ***TFPI*** - ***2***
       ***domain***
                                                             ***TFPI***
                             ***domain***
                                             ***2***
                                                       of
       ***Kunitz*** -type
     disclosed, as are muteins of ***TFPI*** and ***TFPI*** - ***2***
     . Nucleic acid sequences, expression vectors and transformed host cells
     encoding and capable of producing the disclosed
                                                      ***chimeric***
```

proteins and muteins are also disclosed. Finally, methods for prevention and treatment of septic shock ing the \*\*\*chimeric\*\*\* proteins and muteins are disclosed.

muteins are disclosed. ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1996:295080 CAPLUS 124:325361 DOCUMENT NUMBER: Chimeric proteins and muteins of tissue factor pathway TITLE: inhibitors TFPI and TFPI-2 Innis, Michael A.; Creasey, Alba A. INVENTOR(S): Chiron Corporation, USA PATENT ASSIGNEE(S): PCT Int. Appl., 67 pp. SOURCE: CODEN: PIXXD2 Patent DOCUMENT TYPE: English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: APPLICATION NO. DATE PATENT NO. KIND DATE \_\_\_\_\_\_ \_\_\_\_\_ A2 A3 WO 9604378 WO 9604378 WO 1995-US9464 19950725 19960215 19960314 W: AU, CA, JP, MX RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE 19961231 US 1994-286521 19940805 US 5589359 A US 1995-437841 19950509 US 5563123 Α 19961008 US 1995-436175 19950509 19971209 US 5696088 Α AA 19960215 CA 1995-2196290 19950725 CA 2196290 **A**1 19960304 AU 1995-31500 19950725 AU 9531500 AU 710535 B2 EP 776366 A1 19990923 EP 1995-927478 19950725 19970604 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE JP 10503375 T2 19980331 JP 1995-506598 19950725 US 1997-943682 US 6174721 20010116 19971014 US 1994-286521 A 19940805 PRIORITY APPLN. INFO.: US 1995-438184 B1 19950509 WO 1995-US9464 W. 19950725 \*\*\*Chimeric\*\*\* proteins possessing \*\*\*Kunitz\*\*\* -type AB are provided, as are muteins of \*\*\*TFPI\*\*\* and \*\*\*TFPI\*\*\* - \*\*\*2\*\*\* Nucleic acid sequences, expression vectors, and transformed host cells encoding and capable of producing the disclosed \*\*\*chimeric\*\*\* proteins and muteins are also provided. \*\*\*Chimeric\*\*\* proteins were constructed with amino acid sequences capable of binding a cell surface component (glycosaminoglycan, heparin) such as peptide moieties from protease nexin-1, protease nexin-2, antithrombin III, heparin cofactor II, protein C inhibitor, platelet factor 4, bovine pancreatic trypsin inhibitor, and ghilanten-related inhibitors. The \*\*\*chimeric\*\*\* proteins are produced as yeast .alpha.-factor \*\*\*fusion\*\*\* proteins for secretion, or alternatively, may be expressed as a ubiquitin \*\*\*fusion\*\*\* protein. Potential sites for N-liked glycosylation within \*\*\*TFPI\*\*\* (Asn116.fwdarw.Gln, Asn227.fwdarw.Gln) are removed using overlapping PCR and mutations och1, mn1, and alg3 are introduced in transformed yeast cells to prevent the prodn. of .alpha.-1,6-polymannose terminal carbohydrate moieties in the \*\*\*chimeric\*\*\* products. Finally, methods for prevention and treatment of septic shock using the \*\*\*chimeric\*\*\* proteins and muteins are described. => d his (FILE 'HOME' ENTERED AT 07:23:20 ON 04 DEC 2002) FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 07:23:45 ON 04 DEC 2002 T.1 3347 S TFPI T<sub>1</sub>2 221 S TFPI-2 L3 42 S KUNITZ (P) (DOMAIN 1) 32 S KUNITZ (P) (DOMAIN 2) L4

30 S (L1 OR L2) (P) (L3 OR L4)

2 S L5 (P) (CHIMERIC OR FUSION)

L5

```
2 DUPLICATE REMOVE L6_(0 DUPLICATES REMOVED)
L7
=> s glycosaminoglycan
         70335 GLYCOSAMINOGLYCAN
=> s heparin binding domain
          2924 HEPARIN BINDING DOMAIN
=> s protease nexin-1
L10
         728 PROTEASE NEXIN-1
=> s 19 (p) 110
            3 L9 (P) L10
=> s 17 (p) (18 or 111)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L72 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L78 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L80 (P) '
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L82 (P) '
L12
             1 L7 (P) (L8 OR L11)
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     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     07:23:45 ON 04 DEC 2002
           3347 S TFPI
L1
L2
            221 S TFPI-2
             42 S KUNITZ (P) (DOMAIN 1)
L3
             32 S KUNITZ (P) (DOMAIN 2)
L4
L5
             30 S (L1 OR L2) (P) (L3 OR L4)
              2 S L5 (P) (CHIMERIC OR FUSION)
L6
              2 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
L7
          70335 S GLYCOSAMINOGLYCAN
L8
L9
           2924 S HEPARIN BINDING DOMAIN
L10
            728 S PROTEASE NEXIN-1
L11
              3 S L9 (P) L10
L12
              1 S L7 (P) (L8 OR L11)
=> log y
COST IN U.S. DOLLARS
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                                                                SESSION
FULL ESTIMATED COST
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                                                                  38.46
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
                                                                  TOTAL
                                                 SINCE FILE
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